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PP 4/26/06

Amendment to the Specification:

In the Brief Description of the Drawings, please replace the paragraphs describing Figures 5, 6, and 7 with the following amended paragraphs:

FIGURES 5A – 5D [5]show[s] the compounds present in plate 1 of the functional probe library.

FIGURES 6A – 6D [6] show[s] the activity spectrum for Factor Xa that was generated using the compounds in plate 1 of the functional probe library.

FIGURES 7A – 7D [7] show[s] the activity spectrum for fibroblast growth factor receptor 1 (FGFR1) that was generated using the compounds in plate 1 of the functional probe library.

On page 58, please replace paragraphs 1, 2, and 3 with the following amended paragraphs:

A functional probe library is shown in Figures 5A – 5D [5]. A 96 well plate (Plate 1) contained 94 compounds (and two control wells) and included many compounds that are considered useful for providing information about the ligand binding preferences, and thus probable function, of proteins. For example, cofactors such as NAD and ATP are found in wells A4 and A5, respectively. This particular plate also contained a great many metal ion binding conditions to help probe a target protein for metal ion cofactors.

In order to validate the functional probe screen, two known proteins were incubated with the compounds of Plate 1 and were then assayed using the mircoplate thermal shift assay. For example, the activity spectrum obtained for Factor Xa (Enzyme Research Labs) is shown in Figures 6A – 6D [6].

Factor Xa was purchased from Enzyme Research Labs (South Bend, IN). Reactions were prepared in 96-well polycarbonate microtitre plate v-bottom wells. The final concentration of Factor Xa was 1.4 μM (55 ng/mL) in 200 mM Tris-HCl, pH8. The final concentration of 1,8-ANS was 100 μM. The final concentration of each of the molecules tested for binding is shown in Figures 6A – 6D [6]. The contents were mixed by repeated

uptake and discharge in a 100 μL pipette tip. Finally, one drop of mineral oil (Sigma, St. Louis, MO) was added on top of each reaction well to reduce evaporation from samples at elevated temperatures.

On page 60, please replace paragraph 1 and 3 with the following amended paragraphs.

Reactions were prepared in 96-well polycarbonate microtitre plate v-bottom wells. The final concentration of D(II) FGFR1 was 50 μM in 200 mMTris-HCl, pH8 in each well of a 96-well polycarbonate microtitre plate. The final concentration of 1,8-ANS was 100 μM. The final concentration of each of the molecules tested for binding is shown in Figures 7A – 7D [7]. The contents were mixed by repeated uptake and discharge in a 100 μL pipette. Tip. Finally, one drop of mineral oil (Sigma, St. Louis, MO) was added on top of each reaction well to reduce evaporation from samples at elevated temperatures.

The resultant activity spectrum is shown in Figures 7A – 7D [7]. A larger number of compounds were found to stabilize D(II) FGFR1. For example, all of the sugars, D(+)-glucose, D(+)-sucrose, xylitol, and sorbitol were all found to stabilize (and presumably bind) to D(II) FGFR1. This result may be consistent with the known heparin binding properties of this protein. Tri-polyphosphate, a known polyelectrolyte heparin mimic, yielded the largest shift: about 11 C. This result is consistent with the heparin binding properties of this protein (Pantoliano, M.W. et al., Biochemistry 33:10229-10248 (1994).

On page 61, please replace paragraph 2 with the following amended paragraph.

The final concentration of *lac* repressor was 60 μM in 200 mM Tris-HCl, pH8. Reactions were prepared in 96-well polycarbonate microtiter plate V-bottom wells. The final concentration of 1,8-ANS was 100 μM. The final concentration of each of the molecules tested for binding is shown in Figures 7A – 7D [7]. The contents were mixed by repeated uptake and discharge in a 100 μL pipette tip. Finally, one drop of mineral oil (Sigma, St. Louis, MO) was added on top of each reaction well to reduce evaporation from samples at elevated temperatures.